REMARKS

Claims 1-16, 21-29, 31-34, and 37 are pending in the application. No amendments have been made by the present response.

35 U.S.C. §102(e) (Anticipation)

At pages 2-5 of the Office Action, claims 1-4, 6, 7, 9-16, 29, and 37 were finally rejected as allegedly anticipated by Papahadjopoulos et al, U.S. Patent No. 6,803,053 ("Papahadjopoulos").

Applicants respectfully traverse the rejection in view of the following comments.

Independent claim 1 is directed to a microparticle that is less than about 100 microns in diameter and contains: (i) a polymeric matrix; (ii) a lipid having a pKa of less than about 2.5; and (iii) a nucleic acid molecule, wherein the microparticle is not encapsulated in a liposome and the microparticle does not comprise a cell. Independent claim 21 is directed to a microparticle that is less than about 100 microns in diameter and contains: (i) a polymeric matrix; (ii) a lipid having a pKa of less than about 2.5; and (iii) a nucleic acid molecule.

Papahadjopoulos describes lipid:nucleic acid complexes containing, among other components: (a) a cationic lipid; (b) a nucleic acid; and (c) a hydrophilic polymer. Papahadjopoulos describes polyethylene glycol distearoyl phosphatidylethanolamine (PEG-DSPE) as an exemplary hydrophilic polymer that can be used in the complexes disclosed therein.

The claimed microparticles differ from the lipid:nucleic acid complexes disclosed in Papahadjopoulos in several ways. The following remarks renew the arguments presented in applicants' previous response and also address the new comments contained in the current Office Action.

First, the claimed microparticles contain a "polymeric matrix." The Office Action stated at page 3 that "Applicant's own specification defines polymeric matrix as one or more synthetic polymers having solubility in water of less than about 1mg/ml." Applicants respectfully submit that the specification contains no such definition of "polymeric matrix." Instead, the specification states at page 5, lines 19-20 that "[t]he polymeric matrix is made from one or more

synthetic polymers having a solubility in water of less than about 1 mg/l" (emphasis added). The Office Action's characterization of the present specification omitted the important phrase "made from" when referring to a "polymeric matrix." As a result, applicants maintain the assertion that the claimed microparticles are required to contain a "polymeric matrix," not merely a "polymer." A "matrix" is understood in the art to be a material in which something is enclosed or embedded.

There is no indication in Papahadjopoulos that a hydrophilic polymer described therein forms a "polymeric matrix" in the reference's cationic lipid:DNA complexes. Rather, as noted in the passage from Papahadjopoulos cited on page 3 of the Office Action, "the hydrophilic polymer locates and is incorporated into hydrophobic pockets" in the cationic lipid:DNA complex. Although the Office Action has identified a passage in Papahadjopoulos that refers to a "polymer," there is nothing to suggest that this polymer forms a "polymeric matrix" as is required by the claims.

Second, Papahadjopoulos does not disclose a composition containing (i) a polymeric matrix and (ii) a lipid having a pKa of less than about 2.5. The "polymeric matrix" and the "lipid having a pKa of less than about 2.5" are two distinct components that must both be present in the claimed microparticles.

The Office Action cites Papahadjopoulos at columns 3 and 4 as describing lipid:nucleic acid complexes containing a hydrophilic polymer such as PEG-DSPE. It is applicants' understanding that the Office Action asserts that PEG-DSPE constitutes the "polymeric matrix" component of the claimed microparticle (item (i), above). However, the Office Action contains no assertion that, in addition to a hydrophilic polymer, a complex of Papahadjopoulos also contains a second component that is a lipid having a pKa of less than about 2.5. Applicants have been unable to find any composition at columns 3-4 of Papahadjopoulos containing these two distinct components.

Third, claim 1 requires that the claimed microparticle (which is not encapsulated in a liposome and does not comprise a cell) be less than about 100 microns in diameter. Applicants acknowledge that Papahadjopoulos states at column 10, lines 55-56 that "the lipids need not be provided in a liposome." However, Papahadjopoulos contains no disclosure of a non-liposome composition that is less than about 100 microns in diameter. The Office Action cited

Example 15 of Papahadjopoulos as allegedly inherently anticipating the claimed invention. However, Example 15 clearly states that the lipid-DNA microparticles described therein were "prepared as described by Hong et al. (FEBS Lett. 400:233-237, 1997)," a publication by several of the inventors of the present Papahadjopoulos reference. Hong et al. describes the preparation of cationic liposomes, not non-liposome compositions. Because the lipid-DNA complex of Example 15 is a liposome, and liposomes are specifically excluded from the claims, the lipid-DNA complex of Example 15 does not anticipate the microparticle of claim 1.

In view of the foregoing, applicants respectfully submit that Papahadjopoulos does not anticipate any of claims 1-4, 6, 7, 9-16, 29, and 37.

35 U.S.C. §103(a) (Obviousness)

At pages 5-8 of the Office Action, claims 1-4, 6-16, 29, 32-34, and 37 were finally rejected as allegedly unpatentable over Papahadjopoulos taken with Rolland et al., U.S. Patent No. 6,040,295 ("Rolland") and further in view of Lunsford et al., U.S. Published Application No. 2002/0182258 ("Lunsford"). Similarly, at pages 8-10 of the Office Action, claims 1-4, 6, 7, 9-16, 26, 29, 32-34, and 37 were finally rejected as allegedly unpatentable over Papahadjopoulos taken with Rolland and further in view of Mathiowitz et al., U.S. Patent No. 6,677,313 ("Mathiowitz").

At pages 6-7, the Office Action stated that "it would have been obvious for one of ordinary skill in the art to employ known polymeric microparticles such as those disclosed in Lunsford to entrap and enhance the stability of the lipid:nucleic acid:PEG-DSPE complexes of Papahadjopoulos *et al.*" At pages 9-10, the Office Action stated that "it would have been obvious for one of ordinary skill in the art to employ known polymeric microparticles such as those disclosed in Mathiowitz, to entrap the lipid:nucleic acid:PEG-DSPE complexes of Papahadjopoulos *et al.*"

Applicants respectfully traverse the rejection in view of the following comments.

Papahadjopoulos describes cationic lipid:nucleic acid complexes that contain at least two different "targeting moieties" attached thereto (see, e.g., abstract and column 37, lines 1-8). Targeting moieties (such as antibodies, antibody fragments, or hormones) are used by Papahadjopoulos to direct the complex to a specific cell type or location within the body. To be

effective, targeting moieties would need to be on the outer surface of the complex so as to be able to interact with their ligands on particular cell types or at particular locations within the body.

As noted in the passages reproduced above, the Office Action asserted that one of ordinary skill in the art would have used a polymeric microparticle of Lunsford or Mathiowitz to entrap the complex of Papahadjopoulos. In response to this assertion, applicants respectfully submit that the skilled person would have had no reason to make such a modification to a complex of Papahadjopoulos. Entrapment of a targeting moiety-containing complex disclosed by Papahadjopoulos within a composition of Lunsford or Mathiowitz (a modification which the Office Action has proposed) would have been expected to partially or completely mask the targeting moieties of Papahadjopoulos and thereby reduce or eliminate their targeting function. As a result of this expected disruption in bioactivity, the person of ordinary skill in the art would have lacked the requisite suggestion or motivation entrap a complex of Papahadjopoulos within a composition of Lunsford or Mathiowitz. For at least this reason, the cited references do not render obvious any of claims 1-4, 6-16, 29, 32-34, and 37.

At pages 10-12 of the Office Action, claims 21-24, 27, and 31 were finally rejected as allegedly unpatentable over Papahadjopoulos taken with Carson et al., U.S. Published Application No. 2003/0109469 ("Carson"), as evidenced by Adema et al., U.S. Patent No. 6,500,919 ("Adema"). Similarly, at pages 12-15 of the Office Action, claims 21-24, 27, 28, and 31 were finally rejected as allegedly unpatentable over Papahadjopoulos taken with Rolland and Lunsford, and further in view of Carson, as evidenced by Adema.

Applicants respectfully traverse the rejection in view of the following comments.

The Examiner cited Carson as allegedly disclosing "employing a peptide or arrays of peptides known in the prior art in a plasmid expression vector for use as an immunogenic composition" and Adema as disclosing "MHC I binding peptides for use in vaccines." Notwithstanding the Examiner's assertions as to the disclosure of these secondary references, neither Carson nor Adema (taken alone or in combination) add what is lacking in Papahadjopoulos. As detailed above in the response to the section 102(e) rejection, the cationic lipid:nucleic acid complexes of Papahadjopoulos: (i) do not contain a polymer "matrix";

(ii) do not contain both a polymeric matrix and a lipid having a pKa of less than about 2.5; and (iii) do not disclose a non-liposome composition that is less than about 100 microns in diameter. Similarly, as noted above in response to the section 103(a) rejection, the person of ordinary skili in the art would have lacked the requisite suggestion or motivation entrap a complex of Papahadjopoulos within a composition of Lunsford or Mathiowitz. Carson and Adema have been cited only for their disclosure relating to immunogenic compositions and contain no teachings that would have led the person of ordinary skill in the art to modify a composition of Papahadjopoulos so as to overcome one or more of the deficiencies noted above. As a result, the cited references do not render obvious any of claims 21-24, 27, 28, and 31.

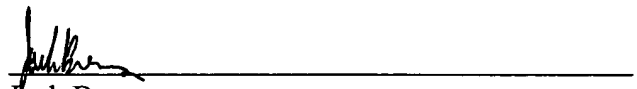
CONCLUSION

Applicants respectfully request that all claims be allowed in view of the remarks contained herein.

Enclosed is a Petition for Extension of Time and a check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 08191-018001.

Respectfully submitted,

Date: November 13, 2006



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